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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
WESSENDORF, T	
ART UNIT	PAPER NUMBER
1627	7

DATE MAILED: 04/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/579,894	Saksela et al
Examiner	**Group Art Unit**
T. Wessendorf	1627

☒ Responsive to communication(s) filed on *2/5/01*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-16* is/are pending in the applicat

Of the above, claim(s) *5-16* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Applicant's election with traverse of Group I, claims 1-4 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that the claims of Groups I-III all share a common feature of the generation of new specific affinities between the SH3 domains and their ligands. Nevertheless, recognize that the claimed structures of the SH3 domains may be different albeit, the binding specificity for the ligand in question is the same. This is not found persuasive because as applicants recognize the structures of the SH3 domains are different Furthermore, restriction is based on the subject matters of Groups I-III being distinct and independent e.g., method and product, not because they share a common feature, especially since if the common feature is the functional property of binding affinity.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-16 are withdrawn from further consideration pursuant to 37 CAR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicants may become aware in the specification.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of generating SH3 domain of the Hck RT-loop, does not reasonably provide enablement for the broadly claimed method for generating the broad SH3 domains RT-loop by replacement with any amino acid residues. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification fails to provide enabling disclosure for the broad scope of the method of generating any SH3 domain by replacing any amino acid residues in any SH3 domain. The specification merely provides generalized statement as to the applicability of the single embodied SH3 domain, Hck to all the

possible SH3 domain containing proteins. There is no reasonable assurance or guidance in the specification that reasonably leads a skilled artisan to extrapolate the method of the instant invention to the different SH3 domains. The scope of the method is too broad since a random RT-loop domain can vary in a number of unpredictable ways such as in the kind of amino acid residues and/or length of the sequence, the correct length or size of the peptide that a particular vector can take to properly display said peptide sequence, the frequency of occurrence of a given amino acid in a library or peptide sequence in a random RT-loop and other undefined and unpredictable factors that affect the generation of one SH3 domain from another. Furthermore, the experimental studies done in the specification (e.g., page 19, lines 9-25) provides other unpredictable effect for already a very specific SH3 domain for Hck and its binding ligand, Nef. The example cleary demonstrates that the binding affinity to SH3 domains by the Nef ligand is governed to a large extent by the nature of the amino acid residues flanking the core sequence. Other peptides are found not to closely adhere to the core sequences. Studies in the art, at present indicate that there is no clear pattern in the occurrence of a ligand motif in a particular protein families, and neither has a proper quantitative determination of binding affinities been carried

out. It still remains to be seen whether the proline-rich peptides are true SH3 ligands inasmuch as there are substantial differences in the identity of the amino acid that make up the receptor site of SH3 domain. Thus, even if it is suggested that the overall structures of the binding sites in the e.g., Src and P13K SH3 domains are similar their ligand properties may differ. The most urgent problem still faced in the art and, apparently similarly encountered by applicants, is to identify proteins that bind to SH3 with high affinity, selectivity and/or specificity. See the Briggs reference (The Jrnl. Of Biological Chemistry) at e.g., page 17901, col. 2 up to page 17902. Also, Collette et al (The Jrnl. Of Biol. Chemistry) at e.g., page 4173, col. 2 up to page 4174, col. 2. Accordingly, it would take an undue amount of experimentation not only to determine a method that is generally applicable for any or all SH3 domain containing proteins. But also, the amino acids that comprised a particular SH3 domain or the consensus sequence responsible for ligand binding to said RT-loop of the SH3 domain. As broad as the claimed method and components use in the method, the claim is nothing more than an invitation to experiment, in the hope that a discovery can be made. In an highly unpredictable and undeveloped art, as therapeutics and peptide, direction or guidance is needed such a skilled in the art would not resort to such. Ex parte Forman, 230 USPQ 546, BPAI, 1986.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). It is not clear as to the difference of step (a) process from step (b). These process steps are the same since the production of a collection of SH3 domains is in actuality the generation of recombinant libraries. Furthermore, it is not clear how a recombinant libraries expresses the RRT-SH3 domains. There seems to be a step missing between steps (a) and (b). Step © is indefinite in the selection process to identify novel SH3 domains. The preamble recites generating not identifying any SH3 domains. Also, the term 'novel' is indefinite. The term tailored is not an art-recognized term. Does the term refer to specific? It is suggested that applicants use term that is art-recognized. Claim 1.

B). The language `is effected' in claim 2 is indefinite as to how said replacement of amino acid residues is effected. `The

variable region of the RT-loop' lacks antecedent basis of support from the base claim 1 which does not recite a variable region.

C). ▒The six amino acids▒ lack antecedent support from the base claim 1. Also, it is not clear within the claimed context, the term `corresponding' .

D). Claim 4 is indefinite as to the recitation that the recombinant libraries are selected from plasmid, phagemid and viral libraries. It is not clear whether the plasmid, phagemid and viral are vectors or libraries.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by Hiipakka et al (J. Mol. Biol.).

The claimed method of producing SH3 domains comprising producing a recombinant libraries that expresses a mutant RT-loop domain of the SH3 regions and affinity selecting the SH3 regions is fully met by the specific process steps of Hiipakka, e.g., at page 1097, col. 2 up to page 1098, col. 2.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lee et al (The EMBO Journal).

Lee et al discloses a method of producing SH3 domain from the RT-loop region of the different SH3 domains. Lee produces said SH3 domain by first mutating some residues of the RT-loop of the different SH3 domains, e.g., page 5010, Fig. 4. The collection of mutant RT-loop region is obtained from a library of cDNA. The RT-loop mutated region is then affinity purified to identify the mutant RT-loop peptide that binds to the PXXP motif of e.g., Nef with specificity and affinity. It is considered that the different mutations of the different SH3 regions of the different kinases is the same to the claimed randomized RT-loop domains or would have been obvious to make into a random collection in view of the Lee's disclosure as to the different

amino acids that can be mutated in the different SH3 domain of the SH3 wild type.

No claim is allowed.

Certain papers related to this application may be submitted to Art Unit 1627 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 O.G. 61 (November 16, 1993) and 1157 O.G. 94 (December 28, 1993)(see 37 C.F.R. 1.6(d)). The official fax telephone numbers of the Group are (703)308-7924. NOTE: If applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. Wessendorf whose telephone number is (703) 308-3967. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

tdw
4/11/01

T.D. W

T.D. WESSENDORF
PRIMARY EXAMINER